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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/608,723

06/26/2003

Andrew R. Marks

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56949 7590 10/30/2007
WilmerHale/Columbia University
399 PARK AVENUE
NEW YORK, NY 10022

EXAMINER

LI, RUIXIANG

ART UNIT	PAPER NUMBER
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1646

MAIL DATE	DELIVERY MODE
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10/30/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/608,723	Applicant(s) MARKS, ANDREW R.	
	Examiner Ruixiang Li	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 43-64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 43-64 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input type="checkbox"/> Other: _____ |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :8/16/2007, 3/5/2007, & 2/13/2007.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/16/2007 has been entered. Claims 1, 3-6, 13, 15-18, 25-42 are canceled. New claims 43-64 are entered and under consideration.

Withdrawn Objections and/or Rejections

All rejections set forth in the previous office action are made moot by cancelled claims.

Information Disclosure Statement

The information disclosure statement filed on 8/16/2007, 3/5/2007, and 2/13/2007 have been considered by the examiner.

Claim Rejections under 35 USC § 112, 1st paragraph

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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(ii). Claims 43-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claims 43-64 are drawn to a method for treating a human subject afflicted with supraventricular tachyarrhythmia or a method for inhibiting the onset of supraventricular tachyarrhythmia in a human subject, comprising administering to the human subject a therapeutically effective amount of JTV-519. The specification discloses that during exercise, PKA phosphorylation of RyR2 partially dissociates FKBP12.6 from the channel, increasing intracellular Ca^{2+} release and cardiac contractility (Experiment Set II, page 64). The specification also discloses that RyR2 channels from FKBP12.6-deficient mice and from patients with catecholaminergic polymorphic ventricular tachycardia (CPVT) are more active during exercise compared to controls and that

cardiomyocytes from FKBP12.6-deficient mice exhibit after-depolarizations that can trigger arrhythmias that cause sudden cardiac death (Experiment Set II, page 64). The specification further discloses that JTV-519 enables FKBP12.6 to bind to PKA-phosphorylated RyR2 in an in vitro binding assay (Experiment Set III, pages 92-93).

However, there are no working example of treating a human subject afflicted with supraventricular tachyarrhythmia or inhibiting the onset of supraventricular tachyarrhythmia in a human subject, comprising administering to the human subject a therapeutically effective amount of JTV-519. The specification does not provide sufficient guidance on how to treat supraventricular tachyarrhythmia or inhibiting the onset of supraventricular tachyarrhythmia in a human subject with JTV-519. There is no sufficient evidence showing that human supraventricular tachyarrhythmia is caused by the PKA phosphorylation-induced dissociation of FKBP12.6 from RyR2. Thus, it would take large quantity of experimentation to determine whether the PKA phosphorylation-induced dissociation of FKBP12.6 from RyR2 is the cause of human supraventricular tachyarrhythmia and whether human supraventricular tachyarrhythmia can be treated or the onset of supraventricular tachyarrhythmia in a human subject can be inhibited with JTV-519 that enables FKBP12.6 to bind to PKA-phosphorylated RyR2 in an in vitro binding assay.

The prior art teaches an inhibitory effect of JTV-519 on experimental atrial fibrillation in Langendorff-perfused guinea-pig hearts (Nakaya et al., *British Journal of Pharmacology*,

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131: 1363-1372, 2000). Specifically, perfusion of carbachol (1 uM) shortened monophasic action potential and effective refractory period, and lowered atrial fibrillation threshold of the guinea-pig hearts. Addition of JTV-519 (1 uM) inhibited the induction of atrial fibrillation by prolonging monophasic action potential and effective refractory period (see, e.g., abstract). The prior art also teach that JTV-519 exerts antiarrhythmic effects against atrial fibrillation and may be useful for the treatment of patients with atrial fibrillation (see, e.g., abstract) or the prevention of atrial fibrillation in patients with ischaemic heart disease (bottom of right column of page 1370). However, the prior art does not teach treating supraventricular tachyarrhythmia or inhibiting the onset of supraventricular tachyarrhythmia in a human subject.

In view of the complexity of the nature of the work related to treating heart disease such as supraventricular tachyarrhythmia, it is unpredictable whether JTV-519 can be used to treat supraventricular tachyarrhythmia or to inhibit the onset of supraventricular tachyarrhythmia in a human subject. Therefore, it would require undue experimentation for one skilled in the art to make and use the claimed invention.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

Ruixiang Li

Ruixiang Li, Ph.D.
Primary Examiner
October 26, 2007

RUIXIANG LI, PH.D.
PRIMARY EXAMINER